PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference MM-VPB60162B	FOR FURTHER ACTION	See Form PCT/IPEA/416
International application No. PCT/IB2004/001283	International filing date *(day/month/year)* 08.04.2004	Priority date *(day/month/year)* 09.04.2003
International Patent Classification (IPC) or national classification and IPC C07D471/04, C07D403/14, A61K31/4375, A61K31/519		
Applicant SB PHARMCO PUERTO RICO INC		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☐ *sent to the applicant and to the International Bureau)* a total of sheets, as follows:
      ☐ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

☒	Box No. I	Basis of the opinion
☐	Box No. II	Priority
☒	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

Date of submission of the demand	Date of completion of this report
09.02.2005	03.03.2005
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Kyriakakou, G Telephone No. +49 89 2399-7835

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/IB2004/001283

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:

   ☐ international search (under Rules 12.3 and 23.1(b))
   ☐ publication of the international application (under Rule 12.4)
   ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

   Description, Pages

   1-36 as originally filed

   Claims, Numbers

   1-13 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☐ The amendments have resulted in the cancellation of:

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

   ☐ the description, pages
   ☐ the claims, Nos.
   ☐ the drawings, sheets/figs
   ☐ the sequence listing *(specify)*:
   ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 11-13 in respect of industrial applicability

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. -

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-13
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-13
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-10
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Claims 11-13 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re item V

Reference is made to the following documents

D1: WO-A-0202549
D2: WO-A-9808846
D3: WO-A-9805661
D4: EP-A-1103553
D5: US-A-2002049207

2. Novelty(Art.33(2)PT)

The present application relates to substituted tetrahydropyrido[2,3-d]pyrimidines, tetrahydroquinazolines,tetrahydroquinolines or tetrahydro naphthyridines.The prior art documents D1-D4 disclose substituteditetrahydropyrido[2,3-d]pyrimidines, tetrahydroquinazolines,tetrahydroquinolines or tetrahydro naphthyridines which differ in the nature of the 4-substituent. The prior art document D5 discloses substituted pyrido[2,3-d]pyrimidines, quinazolines,quinolines or naphthyridines.
The subject matter of the present claims 1-13 can therefore be considered to be novel.

3. Inventive step(Art. 33(3)C)

3.1 The object ofthe present application is to provide compounds which are potent and specific antagonists of CRF receptors and are useful in treating disorders mediated by the said receptors.

3.2. The prior art documents D2 and D3 which disclose compounds coming structurally very close to the claimed ones and having the same pharmacological activity are considered to represent the closest state of the Art.

3.3 The application does not contain any pharmacological data for the alleged activity of the claimed compounds. Furthermore the prior art documents D1 and D2 disclose compounds coming structurally very close and having the same pharmacological activity. In view of the close structural relationship to the compounds disclosed in the prior art documents, it is therefore considered as credible that the claimed compounds

have the same pharmacological activity. Furthermore it is evident from the prior art compounds that variation of the 4-substituens can change only quantitatively the pharmacological activity and yield more or less active derivatives. An inventive step cannot therefore be acknowledged for the present clams 1-13.

3.4 In order to be able to acknowledge an inventive step the Applicant is kindly requested to submit relevant comparative tests with a representative number of prior art D2 and D3 compounds, which should demonstrate that the compounds of the present invention exhibit improved pharmacological activity compared to prior art compounds.

4. Miscellaneous

4.1 The breadth of the claims should be such that all the compounds comprised should present the said properties and/ or advantages or they will be their obvious modifications. Everything falling within a valid claim has to be inventive otherwise the corresponding claim must be amended accordingly.

4.2 The following expressions "stereoisomers", "prodrugs", "aryl", "heteroaryl" have according to he Descriptiona specific meaning; this has to be incorporated in the corresponding claims.

Furhermore the said expressions are vague and indefinite and as such render the scope of the corresponding claims unclear. The said expressions are non-limitative and cannot therefore be considered as obvious generalisation of the examples comprised in the description Additionally they render the said claims speculative in that their scope embraces subject matter not yet explored by the Applicant , the effect of which cannot be readily predetermined or assessed.